

SYSTEMATIC REVIEW OF THE EFFICACY OF ARIPIPRAZOLE FOR THE TREATMENT OF ANOREXIA NERVOSA

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Declaration of interest – Dr Richard Whale has received speaker honoraria from Lundbeck and Otsuka.

BACKGROUND

- Changes in brain dopaminergic function have been implicated in the pathophysiology of anorexia nervosa from both preclinical and clinical studies (Kontis 2012:496-515, Brewerton 2012:398 405)
- Therapeutically, olanzapine has been a focus of clinical research with mixed efficacy findings (Kishi 2012:e757 e66, Brewerton 2012:398 405, Dold Psychotherapy and Psychosomatics 2015)
- Aripiprazole, as a D2 receptor partial agonist, may have additional benefit via dopaminergic modulation and be more favourable in this patient population due to less associated weight gain

AIMS

- To undertake a systematic review of the available literature of the efficacy of aripiprazole in the treatment of anorexia nervosa, in all age groups, clinical settings, languages and genders.

METHOD

- CINAHL, EMBASE, MEDLINE, PsycINFO and the Cochrane database were searched using the search terms Anorexia nervosa, eating disorders, antipsychotics, aripiprazole (and its generics).
- Randomised controlled studies were sought primarily but all study types were included. Enquiries were made with pharmaceutical companies, experts in the field and other relevant researchers.

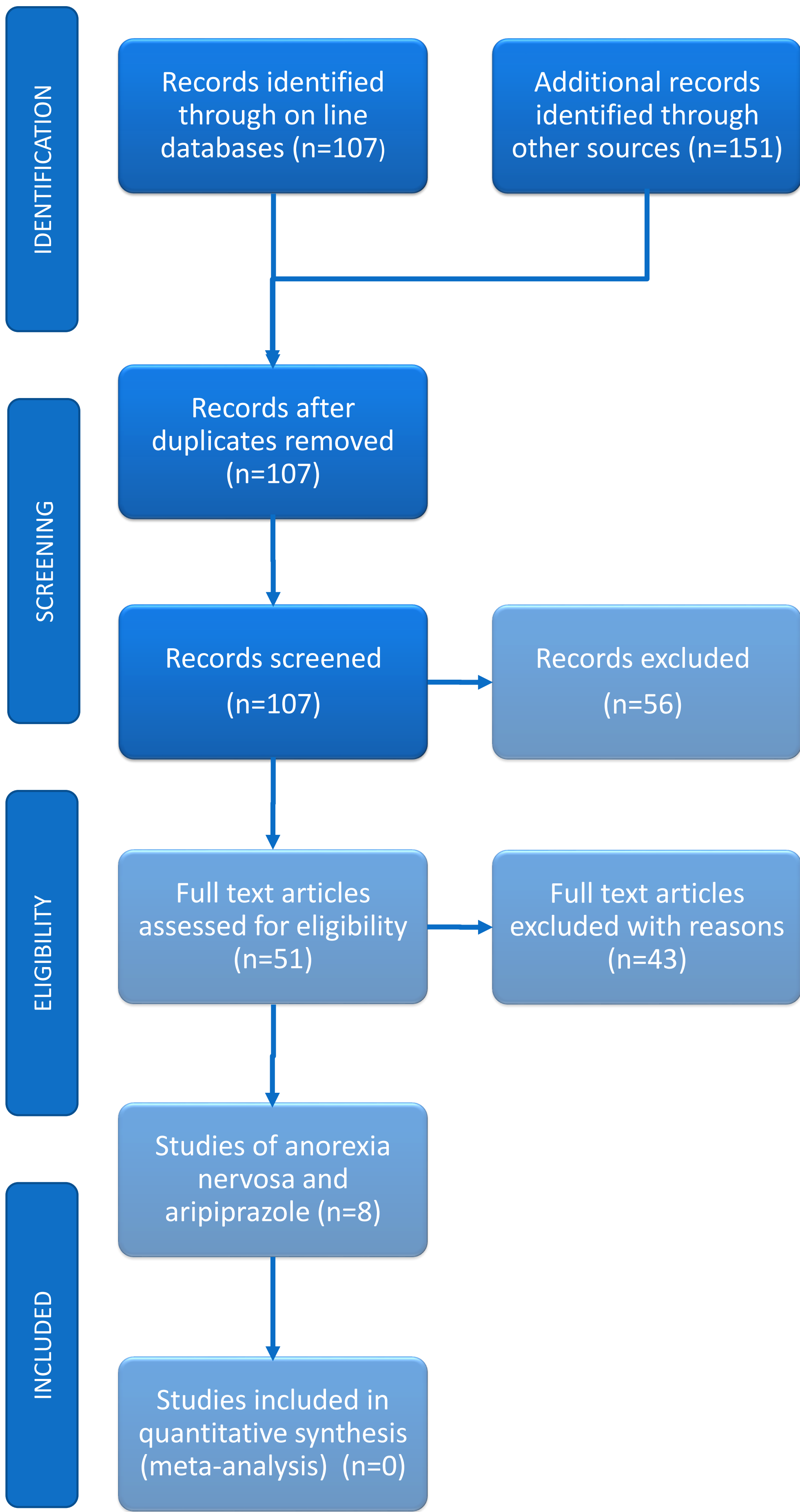
RESULTS

- The only studies available were retrospective chart reviews and case reports/series.
- No published studies met the primary inclusion criteria of randomised placebo controlled trials.
- Results from one proposed randomised study were unavailable and authors did not respond to requests for information/had no further data to add.
- Eight primary reports were found where aripiprazole was used to treat symptoms of anorexia nervosa.
- Aripiprazole showed a positive effect on various eating disorder symptoms including weight gain, binge eating, purging and body image distortion.
- In addition, aripiprazole was observed to aid the refeeding process, increase social functioning, increase insight and was found to be acceptable to the patient group.

CONCLUSIONS

- Whilst positive outcomes for the use of aripiprazole in anorexia nervosa were identified, clear conclusions or recommendations cannot be made due to the inherent reporting bias, small sample sizes and lack of randomisation or blinding in the studies reported.
- Randomised studies are indicated to explore this further.

STUDY SELECTION



REFERENCE & DESIGN	POPULATION	INTERVENTION	COMPARISON	OUTCOME	RISK OF BIAS
Gable 2005 Psychotropic medication use at a : A retrospective chart review and descriptive data analysis.	Anorexia Nervosa N=31/60 Male (8)and Female (23) Age range 12-46 years, mean 20.4 Inpatient (19) and outpatients (12)at private facility	Aripiprazole dose not listed 14/60 12 months study, mean duration of treatment 35 days	Nil	Rated on discharge as improved (achieved ideal body weight, stabilised mood, reduced eating disorder symptoms/achieved remission or reduced suicidal ideation), no change or decompensated from admission. 35% of inpatients on an antipsychotic were rated as improved	Selection bias – high risk Performance bias – high risk Detection bias – high risk
Attia, Kaplan, Scroeder 2005 Open label randomised study	Anorexia Nervosa N=22 Adult outpatients	Aripiprazole	Olanzapine	Nil available	Attrition bias –high risk
Aragona 2007 Tolerability and efficacy of aripiprazole in a case of psychotic anorexia nervosa comorbid with epilepsy and chronic renal failure. Eating and weight disorders 12; 3; e54. Case report.	Anorexia Nervosa N=1 34y Female Outpatient Psychotic Disorder NOS. Epilepsy. Renal failure. Raynaud Syndrome.	Aripiprazole 30mg daily duration 6 months + Carbamazepine + Enalapril + Pipemidic acid + Buflomedil + Sertraline + Risperidone		Weight change 51kg (BMI 18.3) to 52.7 kg SANS and SAPS improved At one year follow up HAM-D =15, HAM-A=9, Y-BOCS=6, BULIT-R=81 At two year follow up HAM-D = 6, HAM-A=6, Y-BOCS=3, BULIT-R=56	Selection bias- high risk Publication bias – high risk
Trunko, Schwartz, Terry 2011 Aripiprazole in anorexia nervosa and low-weight bulimia nervosa: case reports. International journal of eating disorders 44; 3; 269-275 Case report	Anorexia Nervosa N=5 Age range 15-55y Comorbid conditions: Depression NOS, OCD Day Program, Intensive Outpatient program	Aripiprazole 5-10mg Duration 3mths to 18mths Other drugs: Citalopram, Duloxetine, Fluoxetine, Trazadone	Nil	Increase in BMI of 2-4 points (average 3)	Selection bias – high risk Performance bias – high risk
Marzola 2014 Atypical Antipsychotics as Augmentation Therapy in Anorexia Nervosa: Retrospective Chart Review	Anorexia Nervosa total sample 75; N=23 Females on aripiprazole. Mean age 26 Inpatients – Binge/Purge (10) ; Restrictive (13)	3 groups SSRI alone / SSRI +olanzapine / SSRI + Aripiprazole Dose of Aripiprazole 9.13 +/- 6.33mg/day Mean 4.96 +/- 1.62 weeks duration	Olanzapine + SSRI ; SSRI monotherapy	Aripiprazole group: Mean BMI 14.11 to 15.21 Hamilton Rating scale for anxiety, 23.52 to 10; Depression 26.48 to 12.17, Yale-Brown Cornell Eating Disorder Scale Total 18 .84 to 8.64 (large effect size) Ari + SSRI was more effective than Ola + SSRI in treating purging episodes and better than both groups SSRI (p=0.09) and Ola +SSRI (p=0.57) for binges and reduction in YBC-EDS scores	Selection bias –low, Performance bias – high risk Attrition bias- unclear
Launer 2015 Latest Developments in the Psychopharmacology of Anorexia Nervosa Chart review, poster presentation	Anorexia Nervosa Insufficient data provided N=? Age=? Female Inpatient Comorbid OCD, Depression	Aripiprazole + venlafaxine 9 months duration	Nil	Aripiprazole aided refeeding process.	Unclear risk
Contreras 2015 Case report	Anorexia nervosa N=3 Female Adolescents Comorbid Psychosis	Aripiprazole 6 months duration	Nil	Improvement in psychosis and eating disorder symptoms	Selection bias- unclear risk Reporting bias- unclear risk
Guido, Frank 2015 Aripiprazole, a partial dopamine agonist to improve adolescent anorexia nervosa—A case series DOI: 10.1002/eat.22485 Case series	Anorexia Nervosa N=4 Female, Aged 12,12,12,17 Comorbid Separation and social anxiety disorder, GAD, MDD, PTSD Inpatient and outpatient	Aripiprazole 1mg -5mg daily Duration -4 weeks to 12 months Average 28.5 Fluoxetine 10mg, Ativan, Zoloft 50mg	Nil	Weight gain: percentage change in IBW From 8 points to 13 points , average 10.75 Reduced body image distortion N=3 Increased social functioning N=1 increased insight N=1	Selection bias – high risk Publication bias – high risk